REMARKS

Applicant's counsel thanks the Examiner for the detailed action. Originally filed claims 17-33 have been amended so that they better point out and distinctly claim the subject matter which applicant regards as the invention. Support for currently amended claim 17 is fully found in: originally filed claim 18 (which has now been cancelled) and the present specification, see page 1, first paragraph, regarding the carrier being N-vinyl-2-pyrrolidone/vinyl acetate copolymer; the present specification, see page 4, lines 8 and 11, regarding the grinding chamber of a grinding mill; and page 4, line 21, regarding the grinding times between 0.1 to 48 hours. Moreover, support for new claim 34 is fully found in the present specification, see page 4, line 22, regarding the highly preferred grinding times of 0.5 to 8 hours. Such amendments highlight the characterizing features of the invention, i.e. that co-grinding must be carried out only in a specific apparatus (a grinding mill) and that proper times of co-grinding are to be selected, to obtain the product object of the invention, wherein the use of the N-vinyl-2-pyrrolidone/vinyl acetate copolymer results in the inclusion of the active substance on the surface of the carrier.

Thanks to the specific use of a grinding mill, as disclosed by the present specification, in a very simple way it has been obtained that: a) the two powders (both premixed or not) maintain their physical status of solid powder during all the co-grinding process, thus realizing b) the de-structuration of the crystal lattice of the active principle (see specification page 11, lines 31-33). As a result of said de-structuration of the crystal lattice, the active principle micro-crystals are converted into micro- or nano-particles which distribute onto the surface of the micro-particles of N-vinyl-2-pyrrolidone/vinyl acetate copolymer (as demonstrated by the lower melting enthalpies and temperature shown, for example, in Tables 1 to 4 of the present specification).

Neither of these feature are obtainable through the processes described in the prior-art documents cited by the Examiner.

Namely:

Breitenback et al. (US 6,318,650) discloses in claim 1 **[brackets and double emphasis added]**:

> 1. A process for the continuous production of solid, particulate preparations of bioactive substances, in which the bioactive substances are homogeneously **dispersed in a matrix** of thermoplastic auxiliaries, in a **screw extruder** having an extruder jacket, which extruder is divided into a plurality of zones, wherein the process comprises
>
> ***[a)]*** firstly **melting the matrix auxiliaries** and mixing

the bioactive components with the ***[melted]*** matrix auxiliaries in a heatable zone of the extruder to form a **mixture**, and

[b)] subsequently **cooling**, precomminuting and finely grinding the ***[solid]*** mixture in a cooling zone of the extruder to form a powder,

[c)] wherein the screw geometry in the cooling zone is selected so that the cooling zone has a conveying zone as fist zone, followed by a mixing zone and/or a kneading zone.

Moreover, Breitenbach et al. disclose, as correctly pointed out by the Examiner, the use of Kollidon VA 64 as the matrix and ketoprofen as the bioactive substance.

It clearly results that the process of Breitenbach et al. is completely different from the one of the present invention (no simple co-grinding of two substances in a mill, but a very complex procedure, performed in an extruder, which comprises melting at least one of the components is disclosed).

The product obtained by Breitenbach et al. cannot be the same of the present invention. In fact, in step ***a)*** the bioactive component is mixed in melted matrix auxiliaries, i.e. is firstly dissolved inside the matrix. Then, the mixture is cooled giving rise to a solid mixture, which is a solid solution.

Lastly this solid solution is precomminuted and finely ground, i.e. a solid compound (not a powder) is firstly comminuted to give a granulate consisting of granules of the solid solution of above (which consist of the bioactive substance embedded into the solidified matrix), then said granules are finely ground to form a powder, which only consists of micro-granules of the solidified matrix in which the bioactive substance is embedded.

As a matter of fact, contrary to the Examiner's position, it clearly results that no individual separate powders are simultaneously co-ground together, but only granules of a solid solution of an active substance in a matrix.

In view of the above, also the final powder product is different from the one disclosed by Breitenbach et al.

Roser et al. (US 5,958,455) **only** disclose **blending** (**not grinding**, as maintained by the Examiner) of a mixture of substances, comprising a bioactive substance and Kollidon VA 64 (*"...were blended using a Braun coffe grinder for a few seconds..."*).

No specific disclosure, nor even the slightest suggestion exists in Roser et al. that the mixture is somewhat co-ground.

Actually, the very short time (*"...a few seconds "*) applied is a clear disclosure that no grinding happens. That results even more clearly from the fact that the co-grinding process of the present invention at least requires a minimum time of 0.1 hour, up to a maximum of 48 hours, preferably, a minimum time of 0.5 hours. Thus, one of ordinary skill would not have been motivated to select such a short time in the hope of performing the co-grinding process of the present invention.

Czekai et al. (US 5,862,999) only disclose a method of grinding pharmaceutical (i.e. bioactive) substances. No co-grinding at all is disclosed, nor even slightly suggested. Nor, in particular, is disclosed or suggested co-grinding of a bioactive substance with a polymeric carrier (e.g. N-vinyl-2-pyrrolidone/vinyl acetate copolymer) to which the bioactive substance adheres during the co-grinding step.

On the contrary, Czekai et al. **specifically discloses** that polymeric resins (see the exhaustive list of col.2, lines 29-58, wherein N-vinyl-2-pyrrolidone/vinyl acetate copolymer is not cited) can only be **used as grinding media** (no disclosure or suggestion that said polymeric resins can also be use as carriers for the active substance).

Moreover, Czekai et al. **specifically discloses** that the grinding media, i.e. the polymeric resins, **must be separated from the milled particulate** after attrition is completed (see col. 3, lines 65 on), which clearly is not the teaching of the present invention.

In view of the above considerations, none of the above prior-art documents anticipate the subject-matter of currently amended claim 17, nor even slightly suggest it.

Consequently, also the other prior-art documents regarding the compound Kollidon VA 64, which correctly have been cited by the Examiner and which have been precious for ameliorating the general technical knowledge in the field of the various type of Kollidon polymers, are not, nor can be considered relevant prior-art in respect of both novelty and inventiveness of the presently amended claims, neither taken alone nor in combination with the other previously discussed documents.

It can accordingly be seen that the amended claims are now free of the prior art and are appropriately claimed.

For all of the above reasons, the claims as now presented are in condition for allowance, which is respectfully requested.

If any further fees are required by this communication, please charge the same to our Deposit Account No. 16-0820, Order No. BUG5-39330.

Respectfully submitted,

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